

Goldstein et al.
Application No.: 10/045,903
Page 3

PATENT

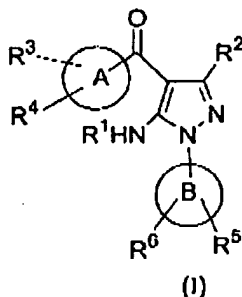
Claim Listing

1. (Canceled)
2. (Canceled)
3. (Currently Amended) The method of Claim ~~33~~ 2 wherein R¹ and R² are hydrogen; and B is phenyl.
4. (Original) The method of Claim 3 wherein A is phenyl.
5. (Original) The method of Claim 4 wherein R⁴ is hydrogen; and R⁵ is halo or alkyl.
6. (Original) The method of Claim 5 wherein R⁵ is chloro, fluoro or methyl; and R⁶ is hydrogen, chloro, fluoro, methyl or methoxy.
7. (Canceled)
8. (Currently Amended) The method of Claim ~~33~~ 7, wherein R³ is pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, N-oxidopyridin-2-yl, N-oxidopyridin-3-yl, N-oxidopyridin-4-yl or pyridon-2-yl, all optionally substituted.
9. (Original) The method of Claim 8, wherein R³ is at the 3-position.
10. (Original) The method of Claim 9, wherein R⁵ is 4-F and R⁶ is hydrogen.
11. (Original) The method of Claim 9, wherein R⁵ is 2-Me and R⁶ is hydrogen.
12. (Canceled)

Goldstein et al.
Application No.: 10/045,903
Page 4

PATENT

13. (Original) The method of Claim 12, wherein R^3 is 3-sulfamoylphenyl, 3-methylsulfonylphenyl, 3-carboxyphenyl or 3-ethoxycarbonylphenyl.
14. (Original) The method of Claim 13, wherein R^3 is at the 3-position.
15. (Original) The method of Claim 14, wherein R^5 is 4-F and R^6 is hydrogen.
16. (Currently Amended) A method of treatment of a disease in a mammal treatable by administration of a p38 MAP kinase inhibitor, comprising administration to the mammal a therapeutically effective amount of a compound of Formula (I):



wherein:

R^1 is hydrogen or acyl;

R^2 is hydrogen or alkyl;

A is an aryl ring;

B is an aryl ring;

R^3 is:

(a) —heteroalkoxy;

(ab) optionally substituted heterocyclalkyl;

(be) optionally substituted heterocyclalkoxy;

(cd) optionally substituted heterocyclalkylamino;

(de) -Y-(alkylene)- R^9 where Y is a single bond, -O- or -NH- and R^9 is optionally substituted heteroaryl, -CONR¹²R¹³, SO₂R¹⁴, -SO₂NR¹⁵R¹⁶, -NHSO₂R¹⁷ or -NHSO₂NR¹⁸R¹⁹ where R¹², R¹³, R¹⁴, R¹⁵, R¹⁶, R¹⁷, R¹⁸ and R¹⁹ are independently of each other hydrogen, alkyl or heteroalkyl;

Goldstein et al.
Application No.: 10/045,903
Page 5

PATENT

- (c) optionally substituted pyridinyl;
- (f) optionally substituted N-oxidopyridinyl; or
- (h) optionally substituted pyridonyl;
- (f) ~~pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, N-oxidopyridin-2-yl, N-oxidopyridin-3-yl, N-oxidopyridin-4-yl or pyridon-2-yl, all optionally substituted; or~~
- (g) ~~3-sulfamoylphenyl, 3-methylsulfonylphenyl, 3-carboxyphenyl or 3-ethoxycarbonylphenyl;~~

R⁴ is:

- (a) hydrogen;
- (b) halo;
- (c) alkyl;
- (d) alkoxy; or
- (e) hydroxy;

R⁵ is:

- (a) hydrogen;
- (b) halo;
- (c) alkyl;
- (d) haloalkyl;
- (e) thioalkyl;
- (f) hydroxy;
- (g) amino;
- (h) alkylamino;
- (i) dialkylamino;
- (j) heteroalkyl;
- (k) optionally substituted heterocycle;
- (l) optionally substituted heterocyclalkyl;
- (m) optionally substituted heterocyclalkoxy;
- (n) alkylsulfonyl;

Goldstein et al.
Application No.: 10/045,903
Page 6

PATENT

- (o) aminosulfonyl, mono-alkylaminosulfonyl or dialkylaminosulfonyl;
- (p) heteroalkoxy; or
- (q) carboxy;

R⁶ is:

- (a) hydrogen;
- (b) halo;
- (c) alkyl; or
- (d) alkoxy;

or a prodrug, individual isomer, mixtures of isomers, pharmaceutically acceptable salt or solvate thereof.

17-24. (Canceled)

25. (Original) The method of Claim 16, wherein R³ is optionally substituted heterocyclalkyl, optionally substituted heterocyclalkoxy or optionally substituted heterocyclalkylamino.

26. (Original) The method of Claim 25, wherein R³ is at the 3-position and is selected from the group consisting of 3-(morpholin-4-yl)propoxy, 2-(morpholin-4-yl)ethoxy, 2-(2-oxo-pyrrolidin-1-yl)ethoxy, 3-(morpholin-4-yl)propyl, 2-(morpholin-4-yl)ethyl, 4-(morpholin-4-yl)butyl, 3-(morpholin-4-yl)propylamino, 2-(morpholin-4-yl)ethylamino, 4-hydroxy-piperidinylmethyl, 2-(S,S-dioxo-thiamorpholin-4-yl)ethyl, 3-(S,S-dioxo-thiamorpholin-4-yl)propyl and N-methylpiperazinylmethyl.

27. (Original) The method of Claim 26 wherein R⁵ is 4-F or 2-Me and R⁶ is hydrogen.

28. (Original) The method of Claim 16 wherein R³ is -Y-(alkylene)-R⁹ where Y is a single bond, -O- or -NH- and R⁹ is optionally substituted

Goldstein et al.
Application No.: 10/045,903
Page 7

PATENT

heteroaryl, $-\text{CONR}^{12}\text{R}^{13}$, $-\text{SO}_2\text{R}^{14}$, $-\text{SO}_2\text{NR}^{15}\text{R}^{16}$, $-\text{NHSO}_2\text{R}^{17}$ or $-\text{NHSO}_2\text{NR}^{18}\text{R}^{19}$ where R^{12} , R^{13} , R^{14} , R^{15} , R^{16} , R^{17} , R^{18} and R^{19} are independently of each other hydrogen, alkyl or heteroalkyl.

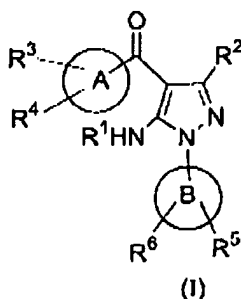
29. (Original) The method of Claim 28, wherein Y is a single bond and R^9 is $-\text{SO}_2\text{R}^{14}$ or $-\text{SO}_2\text{NR}^{15}\text{R}^{16}$.

30. (Original) The method of Claim 29 wherein R^3 is methylsulfonyl or sulfamoyl.

31. (Original) The method of Claim 30 wherein R^5 is 4-F or 2-Me and R^6 is hydrogen.

32. (Canceled)

33. (Currently Amended) A method of treatment of a disease in a mammal treatable by administration of a p38 MAP kinase inhibitor, comprising administration to the mammal a therapeutically effective amount of a compound selected from the group of compounds represented by Formula (I):



wherein:

R^1 is hydrogen or acyl;

R^2 is hydrogen or alkyl;

A is an aryl ring;

B is an aryl ring;

R^3 is: ~~selected from the group consisting of:~~

Goldstein et al.
Application No.: 10/045,903
Page 8

PATENT

- (a) pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, N-oxidopyridin-2-yl, N-oxidopyridin-3-yl, N-oxidopyridin-4-yl or pyridon-2-yl, all optionally substituted; or
- (b) 3-sulfamoylphenyl, 3-methylsulfonylphenyl, 3-carboxyphenyl or 3-ethoxycarbonylphenyl;
- (a) — acylamino;
- (b) — optionally substituted heterocyclyl;
- (c) — optionally substituted aryl or heteroaryl;
- (d) — heteroalkenyl;
- (e) — heteroalkynyl;
- (f) — heteroalkoxy;
- (g) — optionally substituted heterocyclylalkyl;
- (h) — optionally substituted heterocyclylalkenyl;
- (i) — optionally substituted heterocyclylalkynyl;
- (j) — optionally substituted — heterocyclylalkoxy, cyclyloxy, or heterocyclyloxy;
- (k) — optionally substituted heterocyclylalkylamino;
- (l) — optionally substituted heterocyclylalkylearbonyl;
- (m) — NHSO_2R^6 where R^6 is optionally substituted heterocyclylalkyl;
- (n) — $\text{NHSO}_2\text{NR}^7\text{R}^8$ where R^7 and R^8 are, independently of each other, hydrogen, alkyl or heteroalkyl;
- (o) — $\text{Y}(\text{alkylene})\text{R}^9$ where:
- Y is a single bond, O , NH or S(O)_n (where n is an integer from 0 to 2); and R^9 is cyano, optionally substituted heteroaryl, $-\text{COOH}$, $-\text{COR}^{10}$, $-\text{COOR}^{11}$, $-\text{CONR}^{12}\text{R}^{13}$, $-\text{SO}_2\text{R}^{14}$, $-\text{SO}_2\text{NR}^{15}\text{R}^{16}$, $-\text{NHSO}_2\text{R}^{17}$ or $-\text{NHSO}_2\text{NR}^{18}\text{R}^{19}$, where R^{10} is optionally substituted heterocycle, R^{11} is alkyl, and R^{12} , R^{13} , R^{14} , R^{15} , R^{16} , R^{17} , R^{18} and R^{19} are, independently of each other, hydrogen, alkyl or heteroalkyl;

Goldstein et al.
Application No.: 10/045,903
Page 9

PATENT

- (p) $\text{---C(=NR}^{20}\text{)(NR}^{21}\text{R}^{22}\text{)}$ where R^{20} , R^{21} and R^{22} independently represent hydrogen, alkyl or hydroxy, or R^{20} and R^{21} together are $\text{---(CH}_2\text{)}_n\text{---}$ where n is 2 or 3 and R^{22} is hydrogen or alkyl;
- (q) $\text{---NHC(=X)NR}^{23}\text{R}^{24}\text{---}$ where X is O or S, and R^{23} and R^{24} are, independently of each other, hydrogen, alkyl or heteroalkyl;
- (r) $\text{---CONR}^{25}\text{R}^{26}\text{---}$ where R^{25} and R^{26} independently represent hydrogen, alkyl, heteroalkyl or optionally substituted heterocyclalkyl, or R^{25} and R^{26} together with the nitrogen to which they are attached form an optionally substituted heterocycl ring;
- (s) $\text{---S(O)}_n\text{R}^{27}\text{---}$ where n is an integer from 0 to 2, and R^{27} is optionally substituted heterocyclalkyl;
- (t) $\text{---cycloalkylalkyl, cycloalkylalkenyl and cycloalkylalkynyl, all optionally substituted with alkyl, halo, hydroxy or amino;}$
- (u) $\text{---arylaminomethylene or heteroarylaminomethylene;}$
- (v) $\text{---Z-alkylene-NR}^{30}\text{R}^{31}\text{ or Z-alkylene-OR}^{32}\text{---}$ where Z is ---O--- , and R^{30} , R^{31} and R^{32} are independently of each other, hydrogen, alkyl or heteroalkyl;
- (w) $\text{---OC(O)-alkylene-CO}_2\text{H, or OC(O)-NR}^1\text{R}^2\text{---}$ (where R^1 and R^2 are independently hydrogen or alkyl); and
- (x) $\text{---heteroarylalkenylene or heteroarylalkynylene;}$

R^4 is selected from the group consisting of:

- (a) hydrogen;
- (b) halo;
- (c) alkyl;
- (d) alkoxy; and
- (e) hydroxy;

R^5 is selected from the group consisting of:

- (a) hydrogen;

Goldstein et al.
Application No.: 10/045,903
Page 10

PATENT

- (b) halo;
- (c) alkyl;
- (d) haloalkyl;
- (e) thioalkyl;
- (f) hydroxy;
- (g) amino;
- (h) alkylamino;
- (i) dialkylamino;
- (j) heteroalkyl;
- (k) optionally substituted heterocycle;
- (l) optionally substituted heterocyclalkyl;
- (m) optionally substituted heterocyclalkoxy;
- (n) alkylsulfonyl;
- (o) aminosulfonyl, mono-alkylaminosulfonyl or dialkylaminosulfonyl;
- (p) heteroalkoxy; and
- (q) carboxy;

R⁶ is selected from a group consisting of:

- (a) hydrogen;
- (b) halo;
- (c) alkyl; and
- (d) alkoxy; and

prodrugs, individual isomers, mixtures of isomers and pharmaceutically acceptable salts thereof.

34-37. (Canceled)

38. (Previously Presented). The method of Claim 33 wherein the disease is rheumatoid arthritis.

Goldstein et al.
Application No.: 10/045,903
Page 11

PATENT

39. (Previously Presented). The method of Claim 33 wherein the disease is adult respiratory distress syndrome.
40. (Previously Presented). The method of Claim 33 wherein the disease is asthma.
41. (Canceled)
42. (Previously Presented) The method of claim 16, wherein R^3 is optionally substituted pyridinyl, N-oxidopyridinyl or pyridonyl.
43. (Previously Presented) The method of claim 42, wherein R^3 is pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, N-oxidopyridin-2-yl, N-oxidopyridin-3-yl, N-oxidopyridin-4-yl or pyridon-2-yl, each of which may be optionally substituted.
44. (Canceled)
45. (Previously Presented) The method of claim 28, wherein R^3 is $-(\text{alkylene})-\text{SO}_2\text{NR}^{34}\text{R}^{35}$ where R^{34} and R^{35} each independently is hydrogen or alkyl.